Distinguishing Human Cell Types Based on Housekeeping Gene Signatures.

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Public Summary:
Embryonic stem cells cultured in a dish are not homogeneous, but contain different molecular signatures that may predispose them to become one tissue type over another tissue type. In this report, we find that housekeeping genes - those that are always expressed in every cell type - have different expression signatures within different stem cell populations. Using these housekeeping signatures, we can begin to differentiate embryonic stem cells prior to their commitment to particular lineages.

Scientific Abstract:
In this report, we use single cell gene expression to identify transcriptional patterns emerging during the differentiation of human embryonic stem cells (hESCs) into the endodermal lineage. Endoderm specific transcripts are highly variable between individual CXCR4(+) endodermal cells, suggesting that either the cells generated from in vitro differentiation are distinct or that these embryonic cells tolerate a high degree of transcript variability. Housekeeping transcripts, on the other hand, are far more consistently expressed within the same cellular population. However, when we compare the levels of housekeeping transcripts between hESCs and derived endoderm, patterns emerge that can be used to clearly separate the two embryonic cell types. We further compared 4 additional human cell types, including 293T, iPSC, HepG2 and endoderm derived iPSC. In each case the relative levels of housekeeping transcripts defined a particular cell fate. Interestingly, we find that three transcripts, LDHA, NONO and ACTB, contribute the most to this diversity and together serve to segregate all 6 cell types. Overall, this suggests that levels of housekeeping transcripts, which are expressed within all cells, can be leveraged to distinguish between human cell types and thus may serve as important biomarkers for stem cell biology and other disciplines.